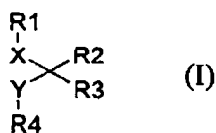


Please amend the application as follows:

In the claims:

This listing of claims will replace all prior versions, and listings, of claims in the application.

1. (currently amended) A compound of general Formula I



or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt,

wherein:

R<sub>1</sub> is selected from the group consisting of:

C<sub>2</sub>-C<sub>6</sub> alkyl, substituted with one or more basic groups, wherein the conjugate acid of said basic group has a pka of from 1 to 15;

cycloalkyl, substituted with one or more basic groups, wherein the conjugate acid of said basic group has a pka of from 1 to 15;

heterocyclyl, comprising at least one nitrogen atom, and substituted with one or more basic groups, wherein the conjugate acid of said basic group has a pka of from 1 to 15;

heterocyclyl, comprising at least one hetero atom selected from S or O, and substituted with one or more basic groups, wherein the conjugate acid of said basic group has a pka of from 1 to 15; and aryl, substituted with one or more basic groups, wherein the conjugate acid of said basic group has a pka of from 1 to 15;

R<sub>2</sub> is selected from the group consisting of H, acyl, acylamino, alkyl, alkylcarbamoyl, alkylthio, alkoxy, aroyl,

arylamino, aryloxy, arylthio, amidino, amino, aryl, carbamoyl, carboxy, cyano, cycloalkyl, formyl, guanidino, halogen, heterocyclyl, hydroxy, oxo, nitro, thiol,

$Z_2N-CO-O-$ ,  $ZO-CO-NZ-$ , and  $Z_2N-CO-NZ-$ ;

$R_3$  is selected from the group consisting of  $COOR_5$ ,  $SO(OR_5)$ ,  $SO_3R_5$ ,  $P=O(OR_5)_2$ ,  $B(OR_5)_2$ ,  $P=OR_5(OR_5)$ , tetrazole, and a carboxylic acid isostere;

$R_4$  represents a  $\begin{array}{c} O-R_5 \\ | \\ -P- \\ || \\ O \end{array} R_6$  -group, or a  $\begin{array}{c} O \\ || \\ -N- \\ | \\ R_7 \end{array} OH$  -group, or a  $\begin{array}{c} O \\ || \\ -O-R_5 \end{array}$  -group,

$R_5$  is H,  $C_1-C_6$  alkyl, or aryl;

$R_6$  is  $C_1-C_6$  alkyl, aryl, cycloalkyl, heterocyclyl, or an optionally N-substituted

$H_2N-C(Z)-CONH-C(Z)-$  or  $H_2N-C(Z)-$  group;

$R_7$  is H or  $C_1-C_6$  alkyl;

X is selected from the group consisting of O, S, SO,  $SO_2$ ,  $C(Z)_2$ ,  $N(Z)$ ,  $NR_7SO_2$ ,  $SO_2NR_7$ ,  $NR_7CO$ , and  $CONR_7$ ;

Y is selected from the group consisting of O,  $N(Z)$ , S,  $C(Z)_2$ , and a single bond; and

Z is independently selected from the group consisting of H,  $C_1-C_6$  alkyl, aryl, cycloalkyl, and heterocyclyl,

with the provisos (1) that when X is O, S, SO,  $SO_2$ ,  $N(Z)$ ,  $NR_7SO_2$ ,  $SO_2NR_7$ , or  $NR_7CO$ , then Y is  $C(Z)_2$  or a single bond and (2) when X is  $CH_2$ , Y is a single bond,  $R_2$  is H,  $R_3$  is  $CO_2H$  and  $R_4$  is  $CO_2H$ , then  $R_1$  is not  $-CH_2CH(OH)$  (1H-1,2,4-triazol-5-yl),  $-CH_2CH(OH)$  (1-trityl-1H-1,2,4-triazol-5-yl),  $-CH_2CH_2NH_2$  or  $-CH_2CH_2$  (1-aminoanthra-9,10-quinone).

2. (currently amended) The compound according to claim 1, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt,

wherein:

R<sub>1</sub> is selected from the group consisting of:

cycloalkyl, substituted with one or more basic groups, wherein the conjugate acid of said basic group has a pka of from 1 to 15;

heterocyclyl, comprising at least one nitrogen atom, and substituted with one or more basic groups, wherein the conjugate acid of said basic group has a pka of from 1 to 15; and

heterocyclyl, comprising at least one hetero atom selected from S or O, and substituted with one or more basic groups, wherein the conjugate acid of said basic group has a pka of from 1 to 15;

R<sub>2</sub> is selected from the group consisting of H, C<sub>1</sub>-C<sub>3</sub> alkyl, amino, halogen, and hydroxy;

R<sub>3</sub> is COOR<sub>5</sub>;

R<sub>4</sub> represents a  $\begin{array}{c} \text{O}-\text{R}_5 \\ | \\ \text{P}-\text{R}_6 \\ || \\ \text{O} \end{array}$  -group,

R<sub>5</sub> is H, C<sub>1</sub>-C<sub>6</sub> alkyl, or aryl;

R<sub>6</sub> is C<sub>1</sub>-C<sub>6</sub> alkyl, aryl, cycloalkyl, heterocyclyl, or an optionally N-substituted

H<sub>2</sub>N-C(Z)-CONH-C(Z)- or H<sub>2</sub>N-C(Z)- group;

X is C(Z)<sub>2</sub>;

Y is O or C(Z)<sub>2</sub>; and

Z is independently H or C<sub>1</sub>-C<sub>6</sub> alkyl.

3. (currently amended) The compound according to claim 1, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt,

wherein:

R<sub>1</sub> is selected from the group consisting of:

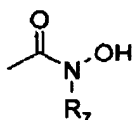
cycloalkyl, substituted with one or more basic groups, wherein the conjugate acid of said basic group has a pka of from 1 to 15;

heterocyclyl, comprising at least one nitrogen atom, and substituted with one or more basic groups, wherein the conjugate acid of said basic group has a pka of from 1 to 15; and

heterocyclyl, comprising at least one hetero atom selected from S or O, and substituted with one or more basic groups, wherein the conjugate acid of said basic group has a pka of from 1 to 15;

R<sub>2</sub> is selected from the group consisting of H, C<sub>1</sub>-C<sub>3</sub> alkyl, amino, halogen, and hydroxy;

R<sub>3</sub> is COOR<sub>5</sub>;

R<sub>4</sub> represents a  -group,

R<sub>5</sub> is H, C<sub>1</sub>-C<sub>6</sub> alkyl, or aryl;

R<sub>7</sub> is H or C<sub>1</sub>-C<sub>6</sub> alkyl;

X is C(Z)<sub>2</sub>;

Y is C(Z)<sub>2</sub> or a single bond; and

Z is independently H or C<sub>1</sub>-C<sub>6</sub> alkyl.

4. (currently amended) The compound according to claim 1, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt,

wherein

R<sub>1</sub> is selected from the group consisting of:

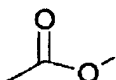
cycloalkyl, substituted with one or more basic groups, wherein the conjugate acid of said basic group has a pka of from 1 to 15;

heterocyclyl, comprising at least one nitrogen atom, and substituted with one or more basic groups, wherein the conjugate acid of said basic group has a pka of from 1 to 15; and

heterocyclyl, comprising at least one hetero atom selected from S or O, and substituted with one or more basic groups, wherein the conjugate acid of said basic group has a pka of from 1 to 15;

R<sub>2</sub> is selected from the group consisting of H, C<sub>1</sub>-C<sub>3</sub> alkyl, amino, halogen, and hydroxy;

R<sub>3</sub> is COOR<sub>5</sub>;

R<sub>4</sub> is a -R<sub>5</sub>-group;


R<sub>5</sub> is H, C<sub>1</sub>-C<sub>6</sub> alkyl, or aryl;

X is C(Z)<sub>2</sub>;

Y is C(Z)<sub>2</sub> or a single bond; and

Z is independently H or C<sub>1</sub>-C<sub>6</sub> alkyl.

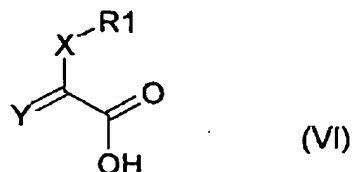
5. (currently amended) A process for the preparation of a compound according to any one of claims 1-4, wherein R<sub>1</sub>, R<sub>5</sub>, R<sub>6</sub>, and Z are as defined in claim 1, R<sub>2</sub> is H, R<sub>3</sub> is COOR<sub>5</sub>,

R<sub>4</sub> represents a -R<sub>6</sub>-group,

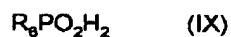
X is C(Z)<sub>2</sub>, and Y is C(Z)<sub>2</sub>,

comprising the step of:

reacting a compound of Formula VI,

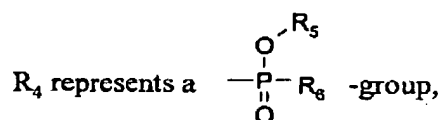


wherein  $\text{R}_1$  and  $\text{Z}$  ~~is~~ are as defined in claim 1,  $\text{X}$  is  $\text{C}(\text{Z})_2$ , and  $\text{Y}$  is  $\text{C}(\text{Z})_2$ , with a compound of Formula IX,



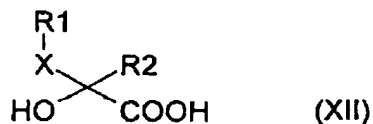
wherein  $\text{R}_6$  is as defined in claim 1, in the presence of a reagent, under standard conditions.

6. (previously presented) A process for the preparation of a compound according to any one of claims 1-4, wherein  $\text{R}_1$ ,  $\text{R}_2$ ,  $\text{R}_5$ ,  $\text{R}_6$ , and  $\text{Z}$  are as defined in claim 1,  $\text{R}_3$  is  $\text{COOR}_5$ ,  $\text{X}$  is  $\text{C}(\text{Z})_2$ ,  $\text{Y}$  is  $\text{O}$ , and



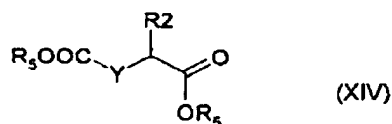
comprising the step of:

reacting a compound of Formula XII,



wherein  $R_6$  is as defined in claim 1, in the presence of a coupling reagent under standard conditions.

7. (withdrawn) A process for the preparation of a compound according to any one of claims 1-4, wherein  $R_1$  and  $R_2$  are as defined in claim 1,  $X$  is  $C(Z)_2$ ,  $Y$  is  $C(Z)_2$  or a single bond, and  $R_3$  and  $R_4$  are  $COOR_5$ , comprising the step of:  
reacting a compound of Formula XIV,

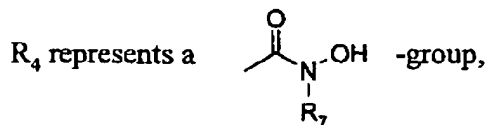


wherein  $R_2$  and  $R_5$  are as defined in claim 1, and  $Y$  is  $C(Z)_2$  or a single bond, with a compound of the general Formula III,

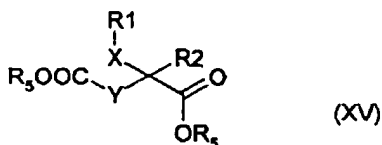


wherein  $R_1$  is as defined in claim 1,  $X$  is  $C(Z)_2$ , and  $L$  is a leaving group, in the presence of a base, under standard conditions.

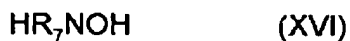
8. (withdrawn) A process for the preparation of a compound according to any one of claims 1-4, wherein  $R_1$ ,  $R_2$ ,  $R_5$ ,  $R_7$ ,  $X$ ,  $Y$  and  $Z$  are as defined in claim 1,  $R_3$  is  $COOR_5$  and



comprising the step of:  
reacting a compound of Formula XV,



with a compound of Formula XVI,



wherein R<sub>7</sub> is as defined in claim 1, in the presence of a reagent under standard conditions.

9. (previously presented) A pharmaceutical formulation comprising a compound according to any one of claims 1-4 as active ingredient in combination with a pharmaceutically acceptable adjuvant, diluent, or carrier.

10. (cancelled)

11. (cancelled)

12. (currently amended) A method for the treatment or prophylaxis of conditions ~~associated with~~ in which inhibition of carboxypeptidase U is required or desired, comprising administering to a patient in need of such treatment an effective amount of a compound according to any one of claims 1-4.



13. (currently amended) A pharmaceutical formulation for the treatment or prophylaxis of conditions ~~associated with~~ in which inhibition of carboxypeptidase U is required or desired, comprising a compound according to any one of claims 1-4 in combination with a pharmaceutically acceptable adjuvant, diluent, or carrier.

14. (withdrawn) A pharmaceutical formulation, comprising:

(i) a compound of Formula I as defined in claim 1 or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt; and

(ii) one or more antithrombotic agents with a different mechanism of action from that of component (i),

in admixture with a pharmaceutically acceptable adjuvant, diluent, or carrier.

15. (withdrawn) A kit of parts comprising:

(i) a pharmaceutical formulation comprising a compound of Formula I as defined in claim 1, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier; and

(ii) a pharmaceutical formulation comprising one or more antithrombotic agents with a different mechanism of action from that of component (i), in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier;

wherein compound (i) and agent (ii) are each formulated for administration in conjunction with the other.

16. (withdrawn) A method for treatment of a patient suffering from, or susceptible to, a condition in which inhibition of carboxypeptidase U and a different antithrombotic mechanism are

required or desired, which method comprises administering to the patient a therapeutically effective total amount of:

- (i) a compound of Formula I, or a pharmaceutically acceptable salt or solvate thereof, or a solvate of such a salt, in admixture with a pharmaceutically acceptable adjuvant, diluent or carrier; and
- (ii) one or more antithrombotic agents with a different mechanism of action from that of component (i), in admixture with a pharmaceutically acceptable adjuvant, diluent, or carrier.

17. (withdrawn) A method for treatment of a patient suffering from, or susceptible to, a condition in which inhibition of carboxypeptidase U and a different antithrombotic mechanism are required or desired, which method comprises administering to the patient a formulation from the kit of claim 15.

18. (previously presented) The compound according to any one of claims 1-4, wherein the basic group is selected from the group consisting of amino, amidino, and guanidino.

19. (withdrawn) The process according to claim 5, wherein the reagent is N,O-bis(trimethylsilyl)acetamide (BSA) or hexamethyldisilazane (HMDS).

20. (previously presented) The process according to claim 6, wherein the coupling reagent is selected from the group consisting of:

- (i) dicyclohexylcarbodiimide (DCC)/N,N-dimethyl amino pyridine (DMAP);
- (ii) (benzotriazol-1-yloxy)tripyrrolidinophosphonium

hexafluorophosphate (PyBop)/ diisopropylethylamine (DIPEA);  
and  
(iii) SOCl<sub>2</sub>.

21. (withdrawn) The process according to claim 7, wherein the leaving group is selected from the group consisting of Cl, Br, I, and tosyl.
22. (withdrawn) The process according to claim 7, wherein the base is lithium diisopropylamide (LDA) or NaH.
23. (withdrawn) The process according to claim 8, wherein the reagent is dicyclohexylcarbodiimide (DCC)/N,N-dimethyl amino pyridine (DMAP).
24. (withdrawn) The formulation according to claim 14, wherein the antithrombotic agent with a different mechanism of action is selected from the group consisting of an antiplatelet agent, thromboxane receptor inhibitor, synthetase inhibitor, fibrinogen receptor antagonist, prostacyclin mimetic, phosphodiesterase inhibitor, and an ADP-receptor (P<sub>2</sub>T) antagonist.
25. (withdrawn) The kit according to claim 15, wherein the antithrombotic agent with a different mechanism of action is selected from the group consisting of an antiplatelet agent, thromboxane receptor inhibitor, synthetase inhibitor, fibrinogen receptor antagonist, prostacyclin mimetic, phosphodiesterase inhibitor, and an ADP-receptor (P<sub>2</sub>T) antagonist.
26. (withdrawn) The method according to claim 16, wherein the antithrombotic agent with a different mechanism of action is

selected from the group consisting of an antiplatelet agent, thromboxane receptor inhibitor, synthetase inhibitor, fibrinogen receptor antagonist, prostacyclin mimetic, phosphodiesterase inhibitor, and an ADP-receptor ( $P_2T$ ) antagonist.